

Causerie over Anesthesie

Vanuit de geschiedenis naar de
digitale kwantumnarcose

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UZ Gent

Dienst Anesthesie

Before anesthesia there was AGONY

- Anesthesia allows progression in surgery
- A most remarkable step forward in medicine

that was the name thereof.

20 And Adam ¹¹gave names to all cattle, and to the fowl of the air, and to every beast of the field; but for Adam there was not found an help meet for him.

21 And the LORD God caused a deep ^lsleep to fall upon Adam, and he slept: and he took one of his ribs, and closed up the flesh instead thereof;

22 And the rib, which the LORD God had taken from man, ¹²made he a woman, and ^mbrought her unto the man.

23 And Adam said, This is now bone



Serratura.







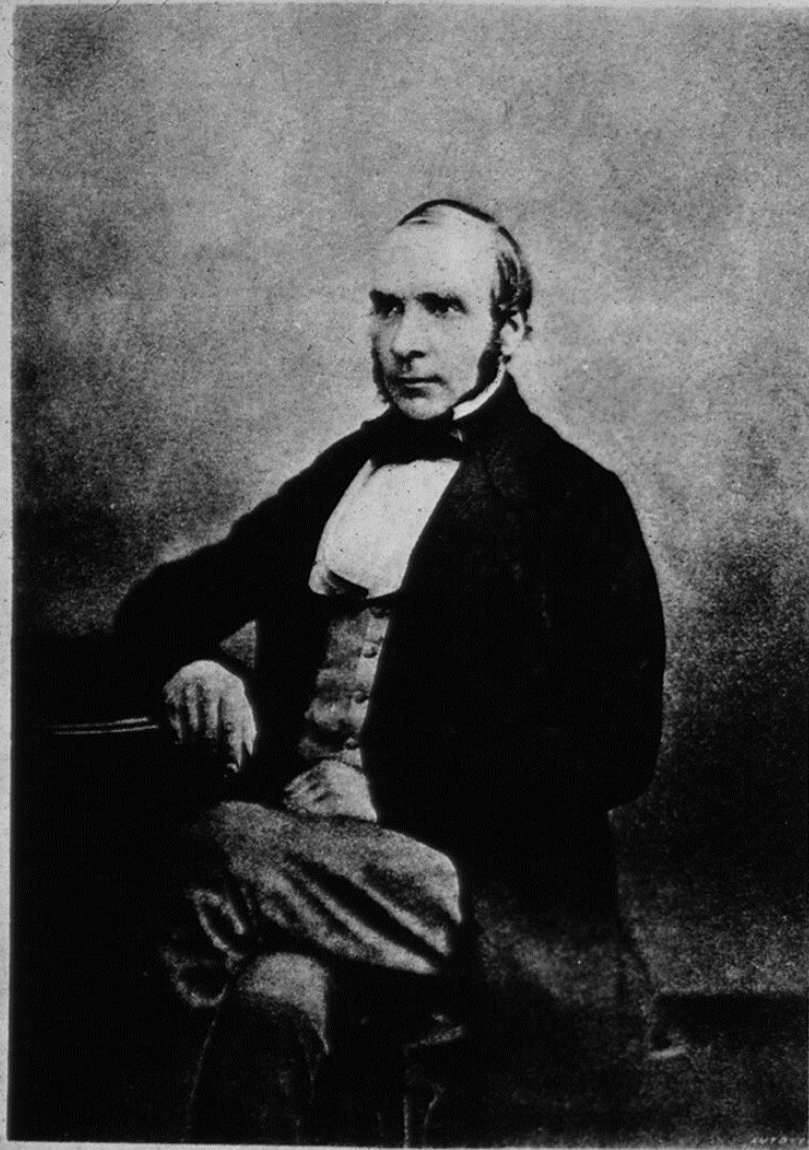
The history of anesthesia



- <<< : opium juice - Mandragora
- 1799 : Davy ontdekt N_2O (laughing parties)
- 1818 : Horace Wells : N_2O in dentist practice with demonstration in Boston (failure)
- 1846 : Morton : succesfull demonstration of anesthesia with aether
Simpson : application of aether for pain relief during labor
→ change towards chlorophorm ("chlorophorm à la reine")
- 1863 : better application of N_2O together with O_2
- 1874 : Ore (Bordeaux) and Deneffe Van Wetter (Gent) : first use of IV anesthetics (chloral)
- 1932 : Weese : IV anesthesia with Evipan
- 1942 : Griffiths : introduction of curare in anesthesia practice



The first public demonstration of surgical anaesthesia, Massachusetts
General Hospital, Boston, October 16th, 1846

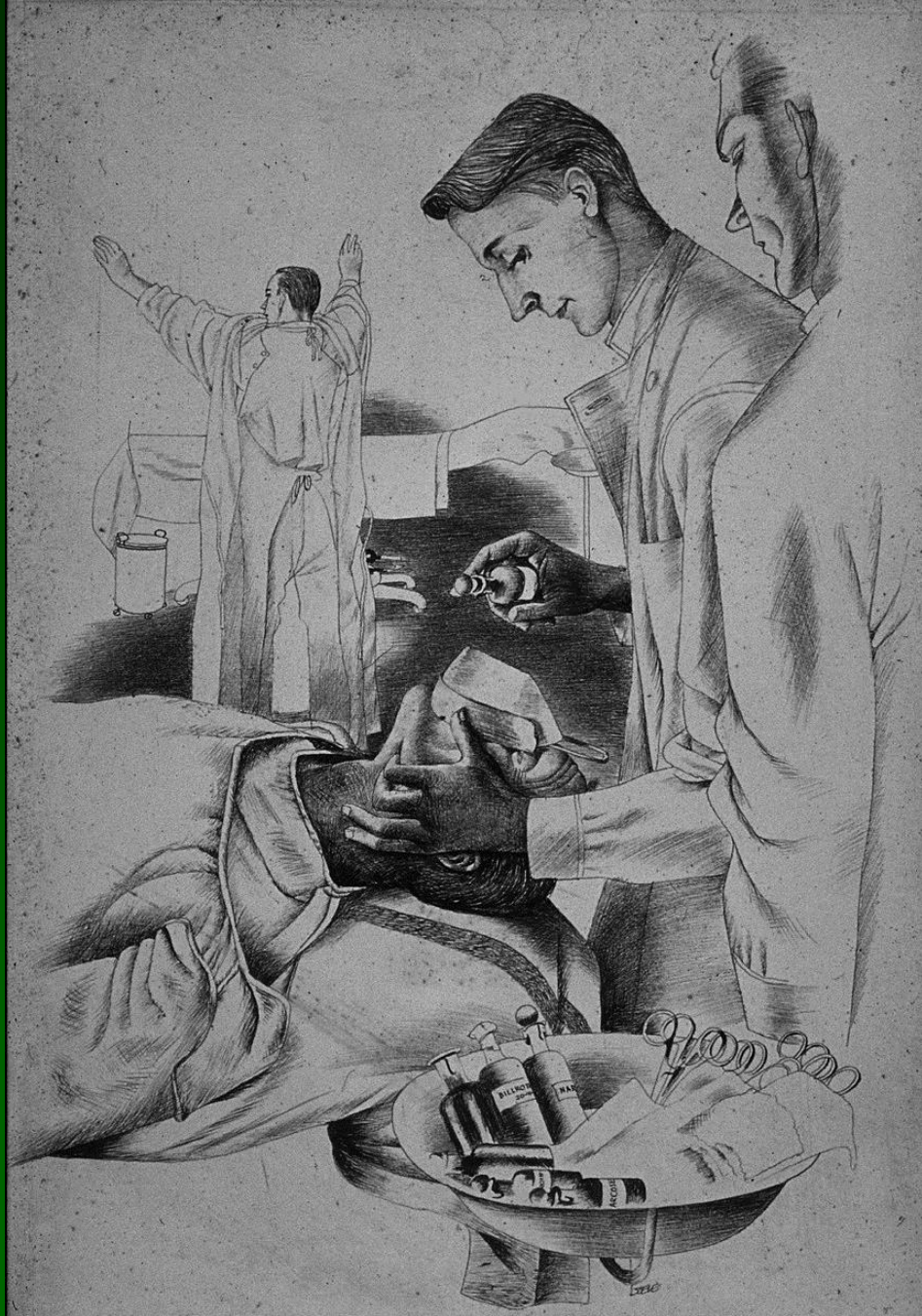


John Snow

[FIG. 14] JOHN SNOW, the first physician to devote his full time to anesthesia. Reproduced from the *Asclepiad*, 1887, vol. 4.



[FIG. 17] Queen Victoria in 1855. Reproduced from Lorne, V.
R. I.: *Queen Victoria—her life and empire.*
Harper & Brothers, 1902.



SIGNS OF GENERAL ANESTHESIA					
	Somatic Muscles	Respiration Thoracic-Diaphragmatic ← Inspiration → → Expiration ←	Oculo-Motor Muscles	Lid Reflex	Pupil Remedication None Morphine
1st Stage Analgesia	Normal Tone			+	○ •
2nd Stage Delirium or Excitement	Uninhibited Activity (or rest)		↔	+	⊙ (reflex dilation)
3rd Stage Surgical Anesthesia	Relaxation		↔	○	○ •
	1st Plane		↔	○	○ •
	2nd Plane		x	○	○ •
	3rd Plane		x	○	○ ○ (Paralytic dilation)
4th Plane	3 Marked	x	○	○ ○	
4th Stage Respiratory Paralysis	4 Extreme			○	○ ○
Anoxemia (Extreme)	Convulsive twitchings or flaccid	Spasm	x x x	open or closed	○ ○

Figuur 1.1 : Schema van Guedel uit 1937 die klinische tekenen van algehele anesthesie bevat (1).

Battleships USS WEST VIRGINIA
and USS TENNESSEE after
the Japanese attack on
Pearl Harbor on Dec. 7, 1941



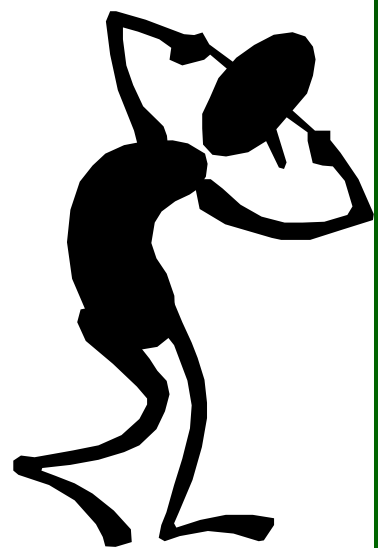
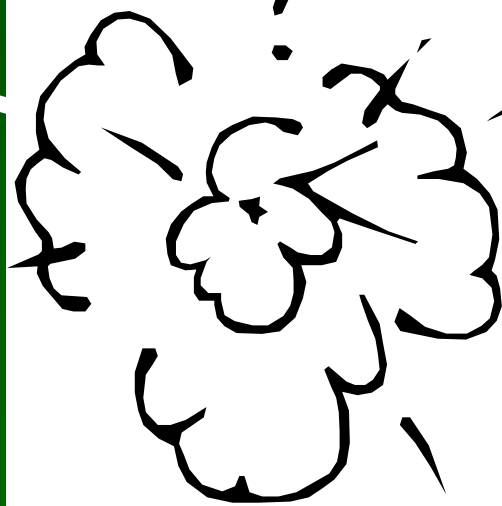
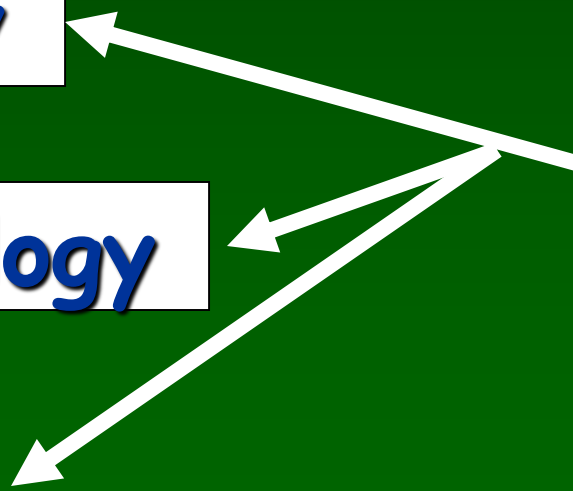


Anesthesia

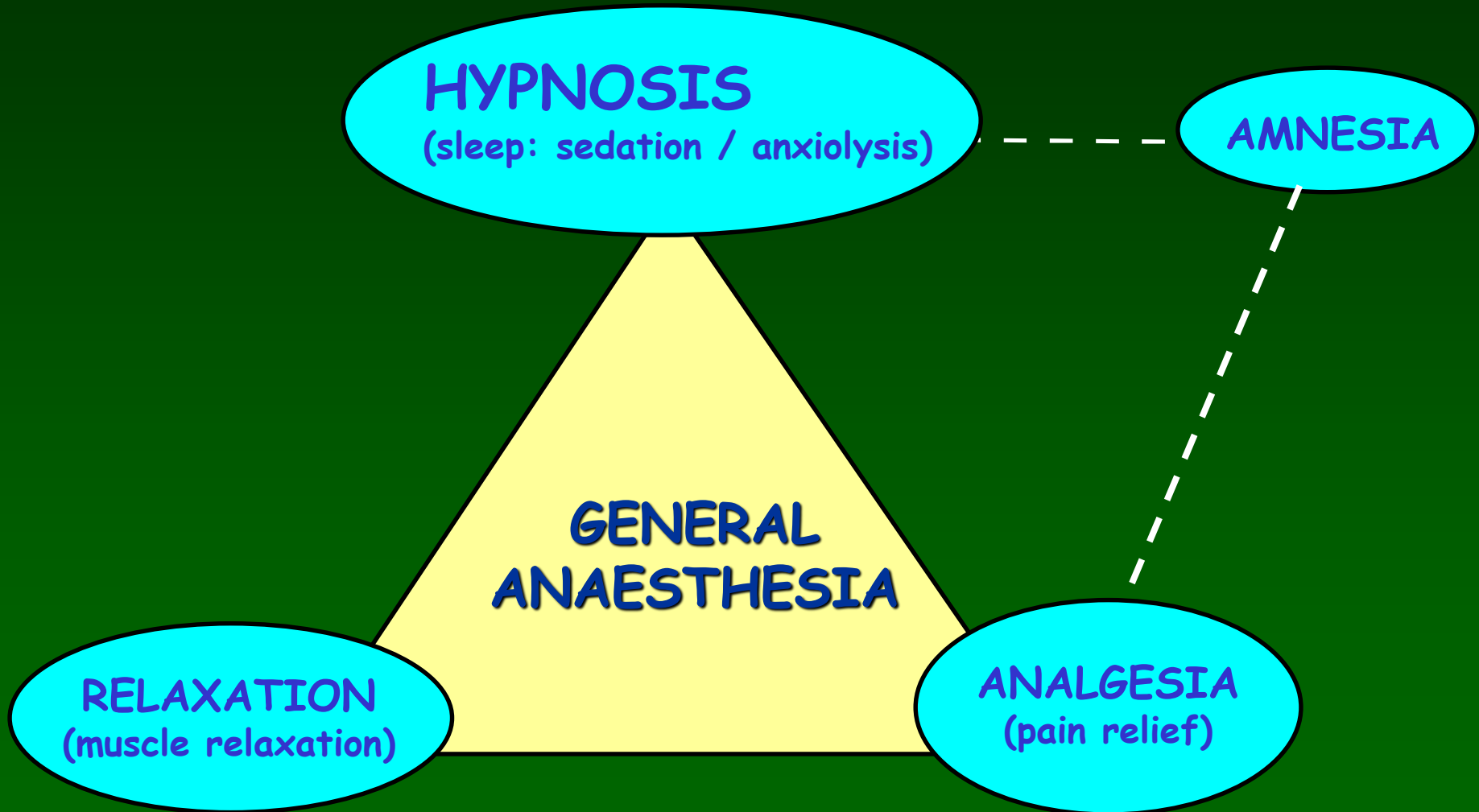
Physiology

Pharmacology

Anatomy



"Triad" Of Anaesthesia









DRUGS

anaesthetic-hypnotic



Propofol

Pentothal

Etomidate

Diazepam
Midazolam

Halothane
Enflurane
Isoflurane
Sevoflurane
Desflurane
N₂O

analgetic



morphine

fentanyl
sufentanil

alfentanil
remifentanil

muscles relaxans



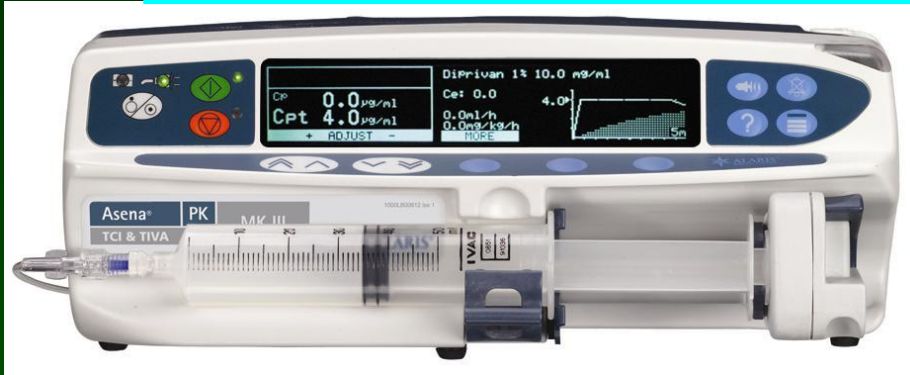
pancuronium
vecuronium
atracurium
cis-atracurium

rocuronium
mivacurium

succinylcholine



So...if we have a TCI or TCA system and a DOA-monitor, we can optimize drug titration



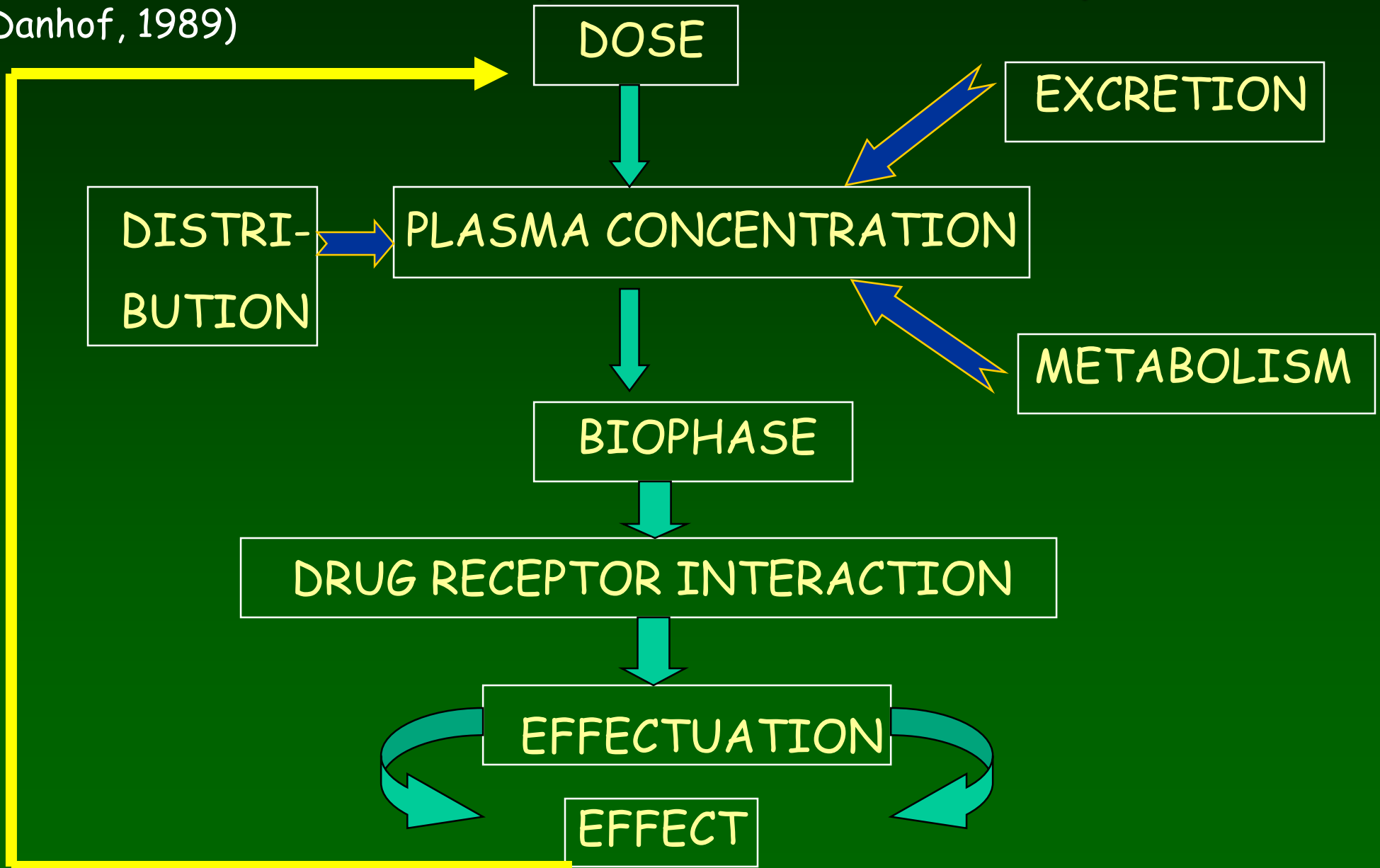


Dose - response relationship

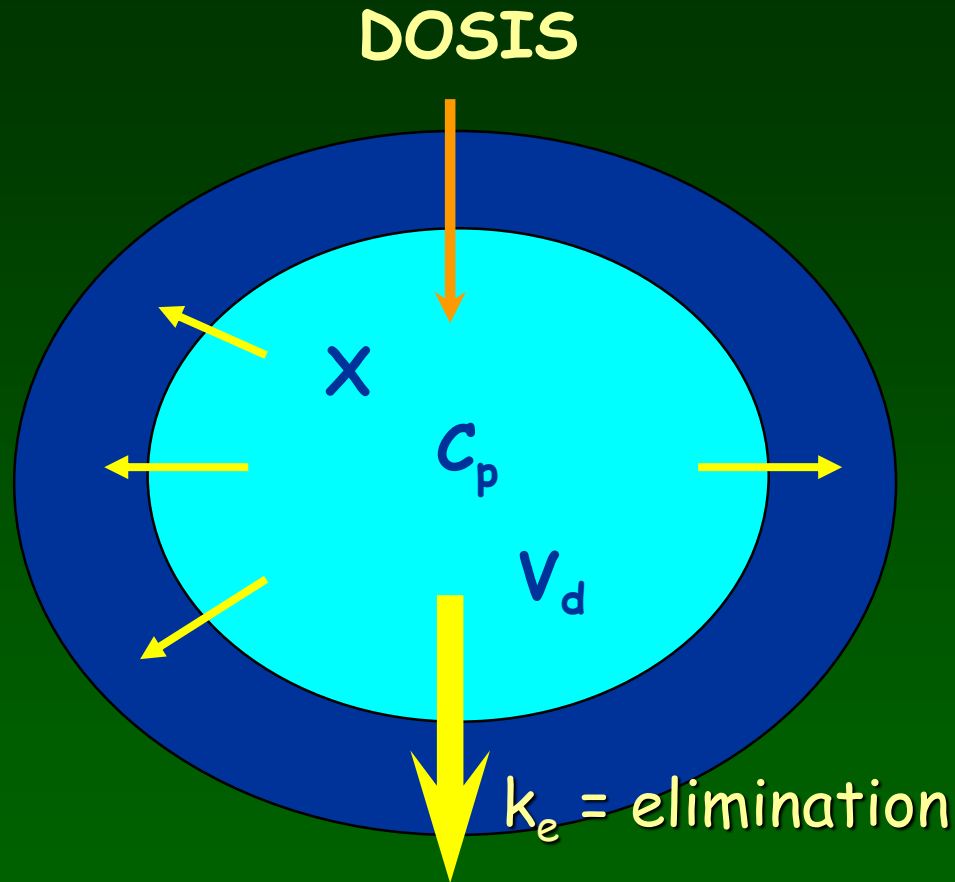
(Danhof, 1989)

F
E
E
D
B
A
C
K

C
O
N
T
R
O
L



1-compartmental model



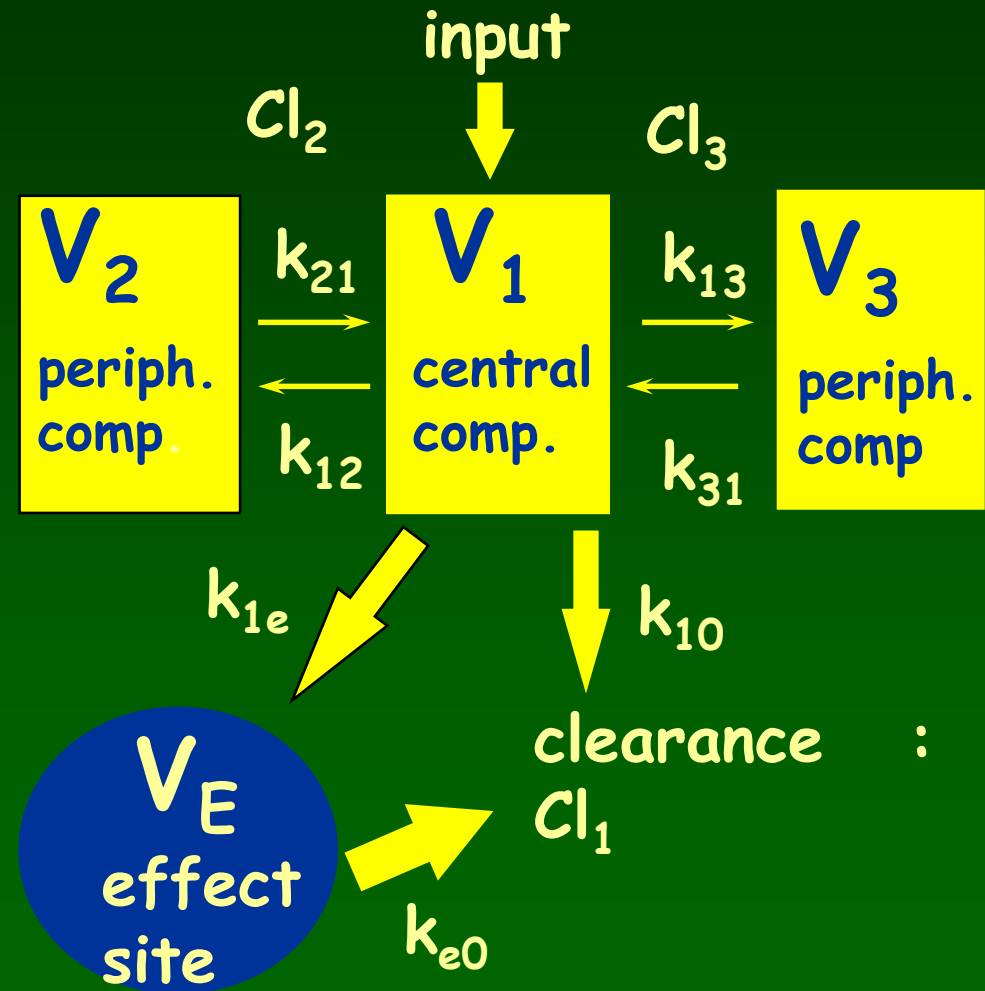
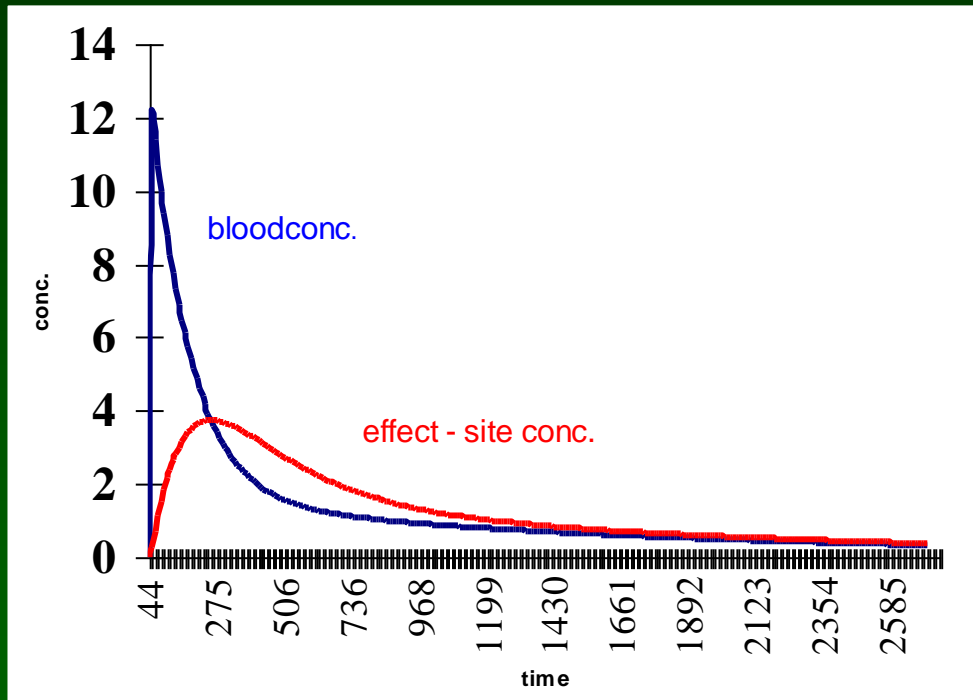
X = amount of drug

C_p = plasma concentration

V_d = volume of distribution

**DISTRIBUTION
PHENOMENON**

Three compartment model with effect site:



DRUGS

anaesthetic-hypnotic



Propofol

Pentothal

Etomidate

Diazepam
Midazolam

Halothane
Enflurane
Isoflurane
Sevoflurane
Desflurane
N₂O

analgetic



morphine

fentanyl
sufentanil

alfentanil
remifentanil

muscles relaxans



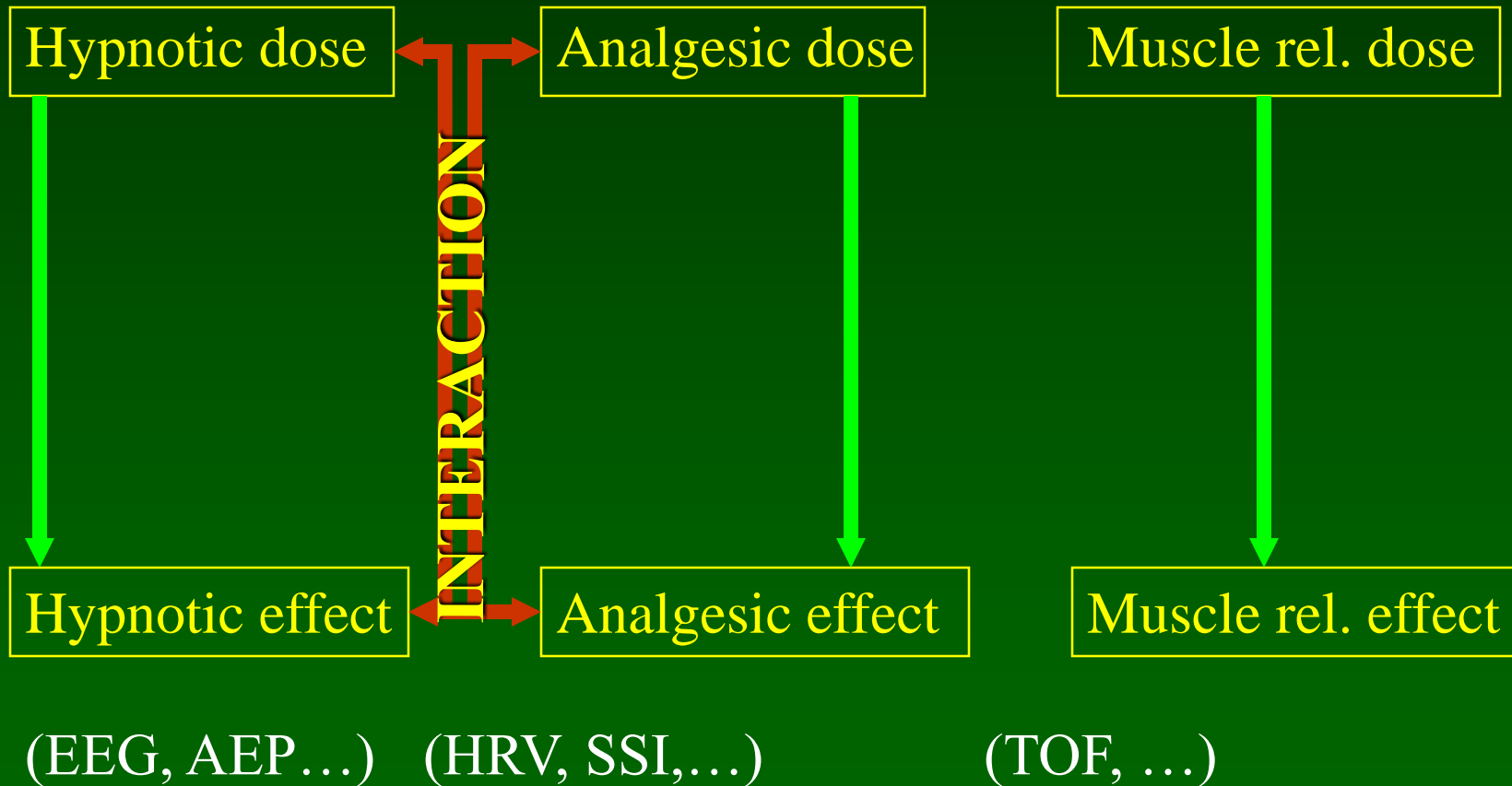
pancuronium
vecuronium
atracurium
cis-atracurium

rocuronium
mivacurium

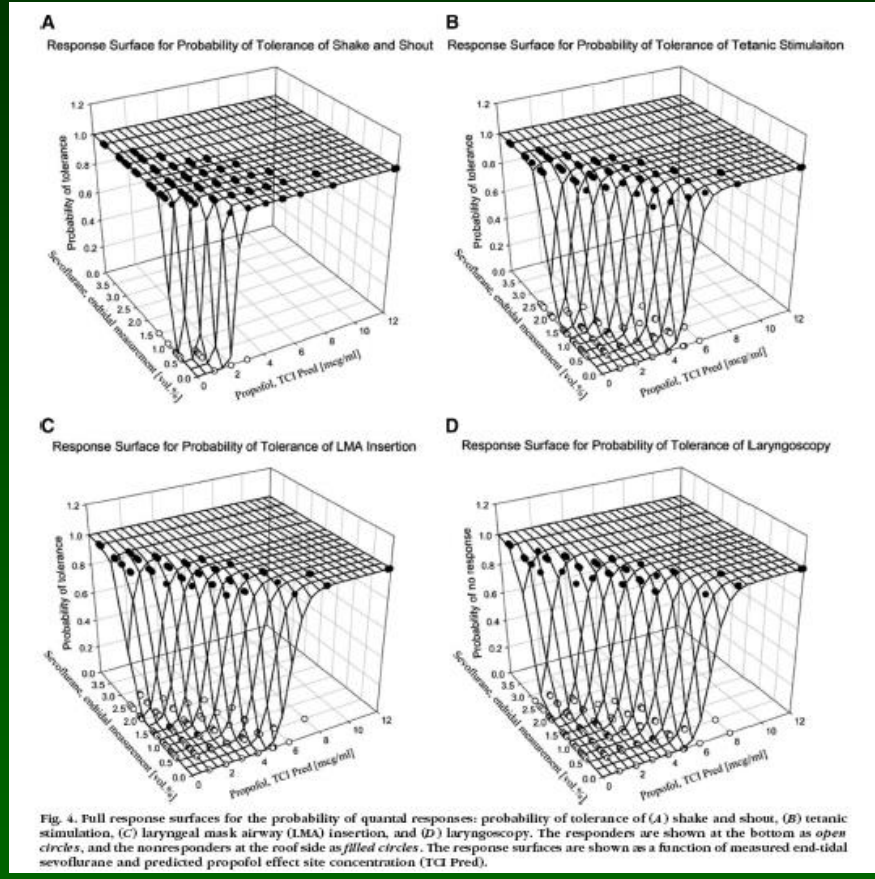
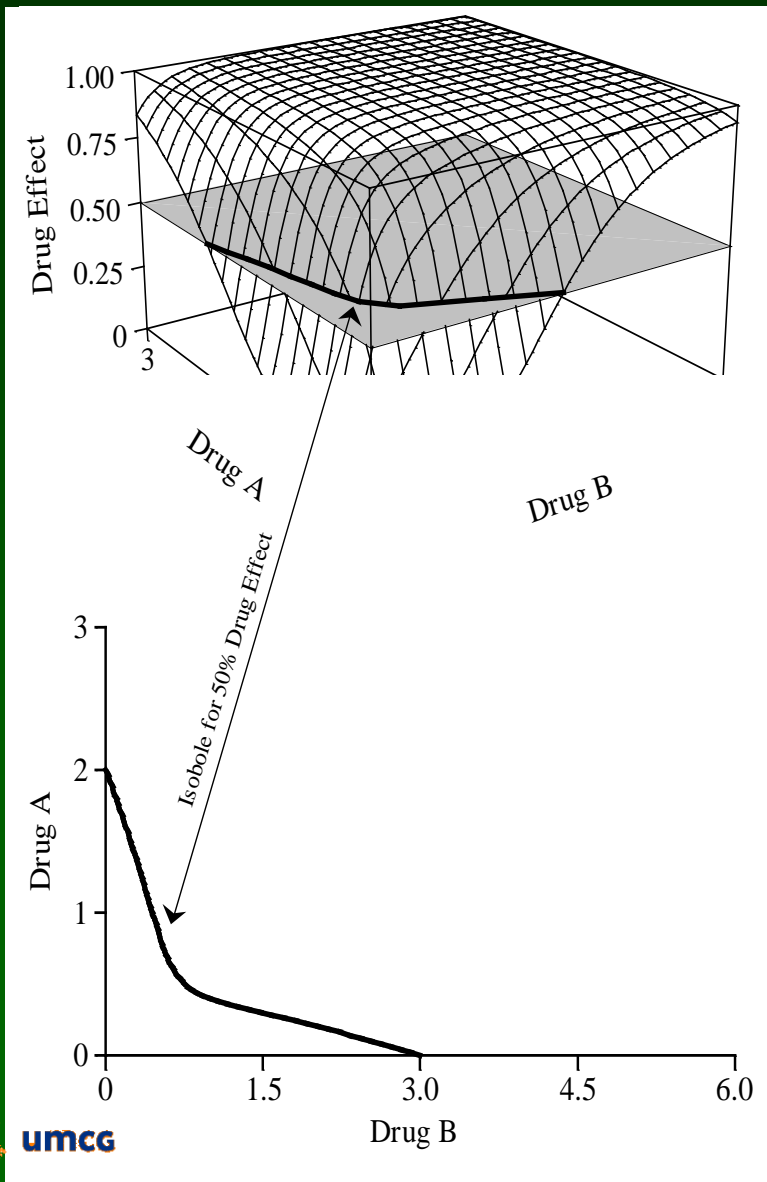
succinylcholine



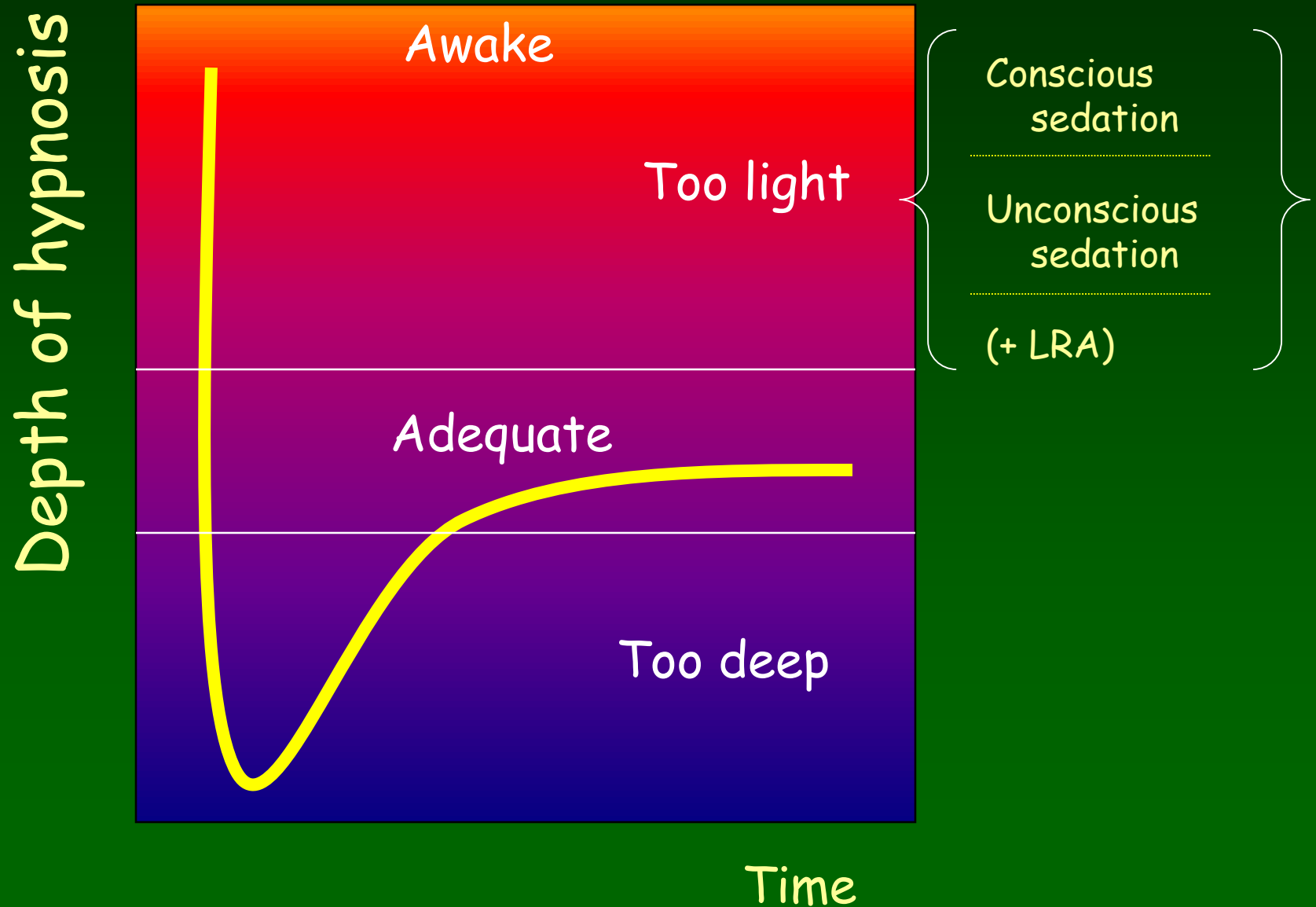
Taking into account interactions



Taking into account interactions



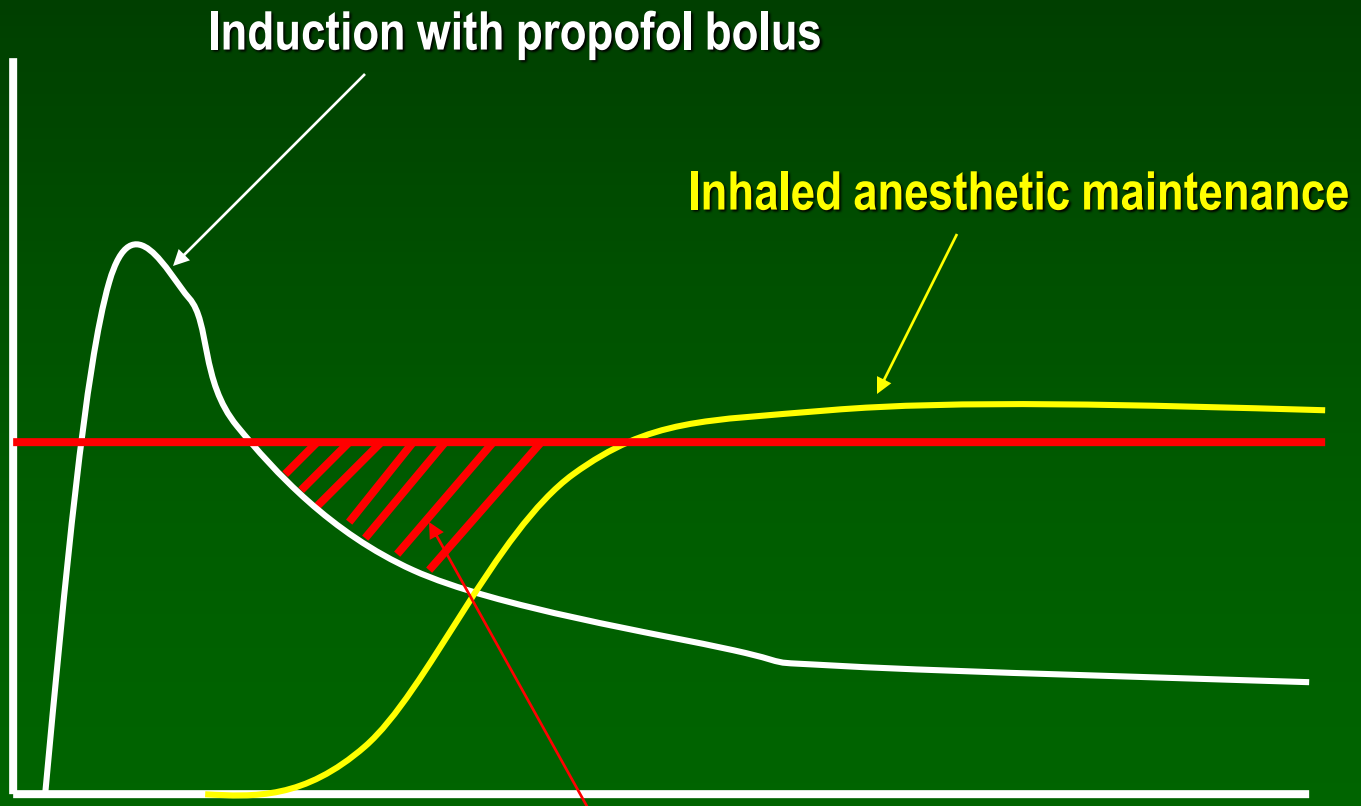
The continuum of anesthetic depth



Preventing the post-induction “Valley of no anaesthesia”



“Depth of anaesthesia”



Application of pharmacokinetics in the obese patient

British Journal of Anaesthesia **91** (5): 638–50 (2003)
DOI: 10.1093/bja/aeg236

BJA

Optimization of desflurane administration in morbidly obese patients: a comparison with sevoflurane using an ‘inhalation bolus’ technique

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Obesity Surgery, **16**, 728-733

Postoperative Results after Desflurane or Sevoflurane Combined with Remifentanil in Morbidly Obese Patients

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Werking

- Lipidentheorie
 - An in fosfolipiden van celmenbraan
 - An kracht ~ vetoplosbaarheid
- NMDA receptoren / complexen
 - An moduleren NMDA activiteit
 - Activiteit van NMDA complex ~bewustzijn / an

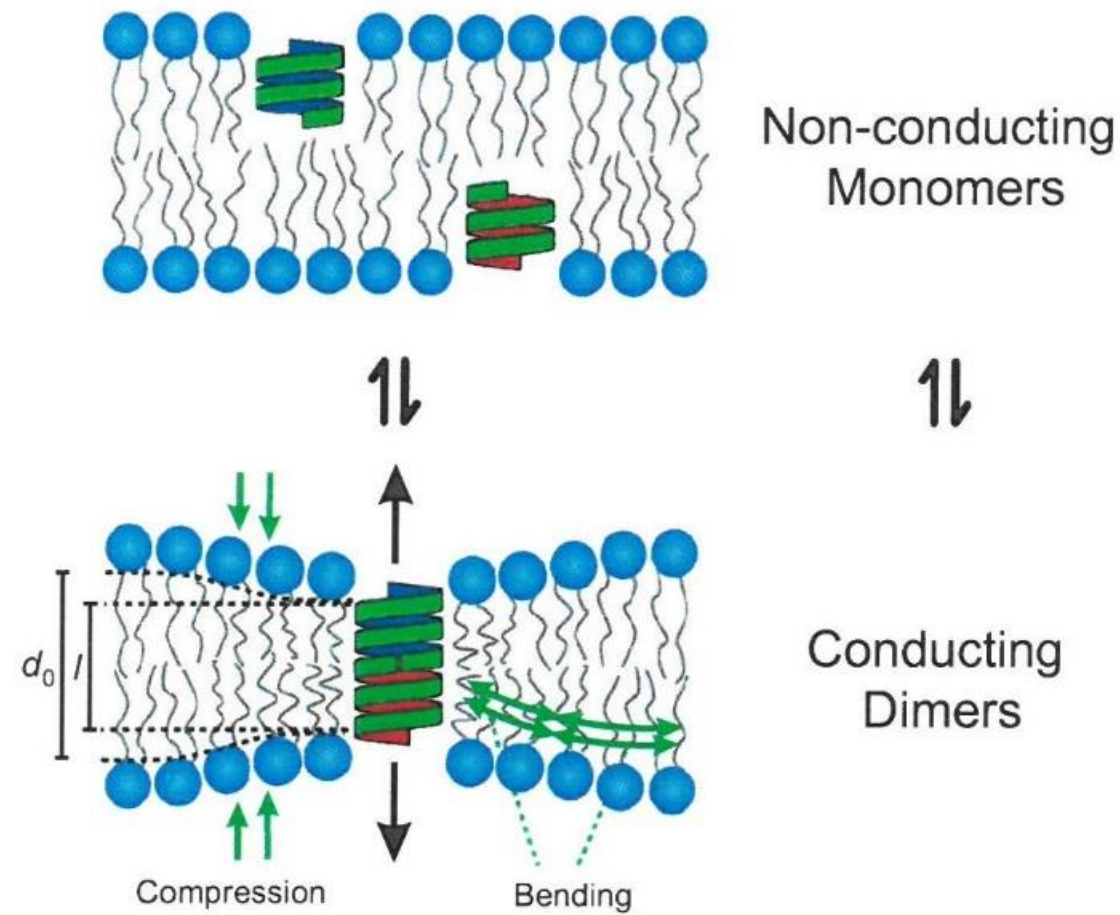


Fig. 1 Schematic of gramicidin channels as molecular force probes for sensing changes in bulk lipid bilayer properties. Two non-conducting gramicidin monomers (*green cylindrical structures*) can dimerize to form a conducting dimer. The thickness of the bilayer (d_0) is larger than the length of the conducting dimer (l), therefore a bilayer deformation energy is required to enable this dimerization. Amphiphiles—compounds with both hydrophilic and lipophilic properties—can lead to changes in bulk bilayer properties that can be sensed by gramicidin channels

Werking

- GABA receptor in nucleus reticularis bepaalt effect op thalamus en cortex
- GABA receptor vooral voor intraveneuse An
- μ receptor voor narcotica/ morfinomimetica

Werking

- **Kwantummechanica**
 - Electromagnetische Van der Waalskrachten
 - een alles of niet en niets daartussen
 - An richten zich op hydrofobe pockets van Tubuline
 - Thalamo corticale netwerken en switchen
 - Xenon een isomeer actief An

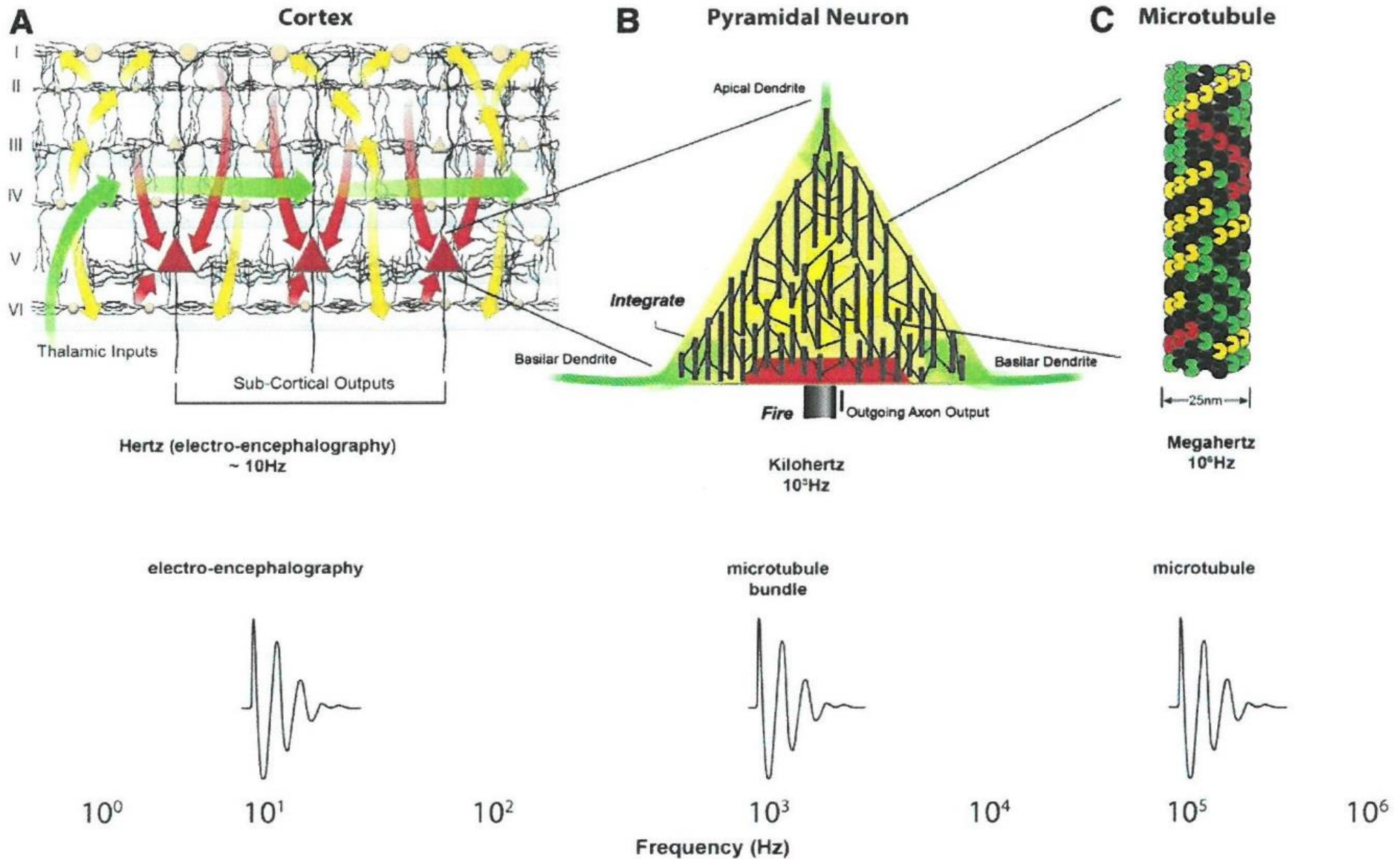


Fig. 1. Top three levels in a six-level recursive brain hierarchy. (A) Cerebral cortex, with thalamic inputs processed in three waves through six cortical layers before converging on layer V pyramidal neurons. (B) Cell body of pyramidal neuron with internal networks of microtubules. (C) Single microtubule comprised of peanut-shaped tubulin proteins.

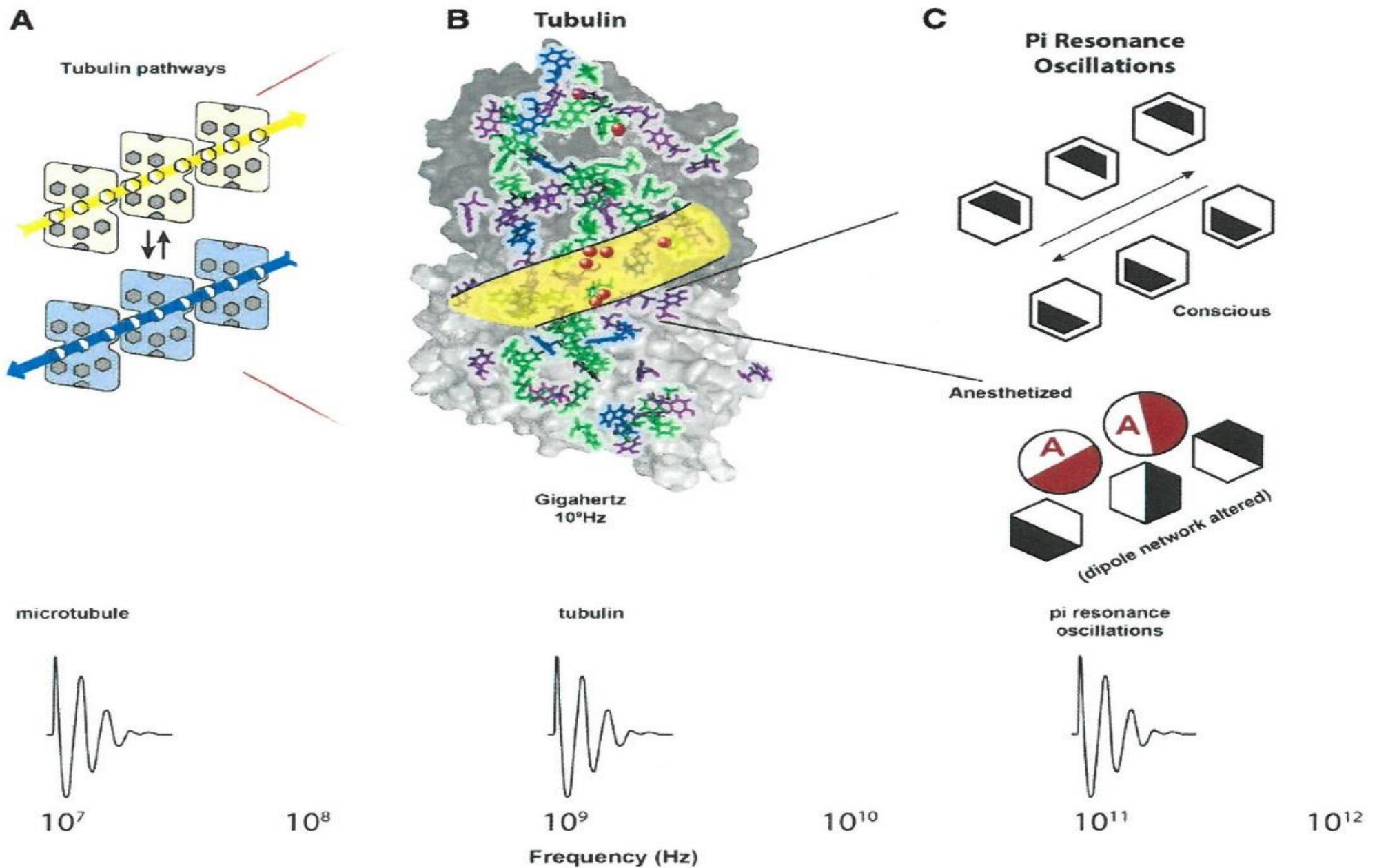


Fig. 2. Lower three levels in a six-level recursive brain hierarchy. (A) Schematic row of three tubulins with oscillating dipole states. (B) Single tubulin with its 86 π resonance rings (*red spheres* indicate anesthetic binding sites). (C) Schematic row of π resonance clouds with dipole states. (Bottom) Anesthetic dampens π resonance dipole oscillations.

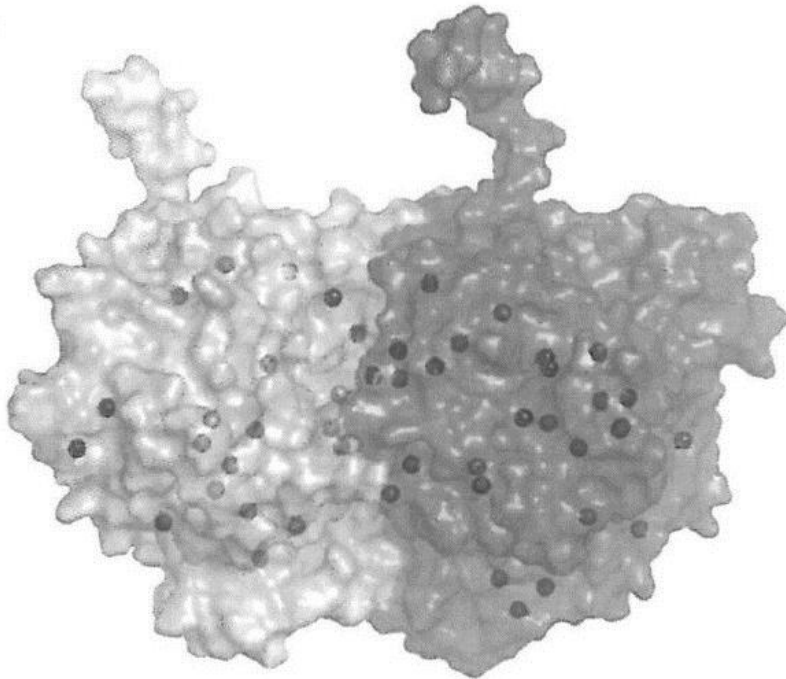
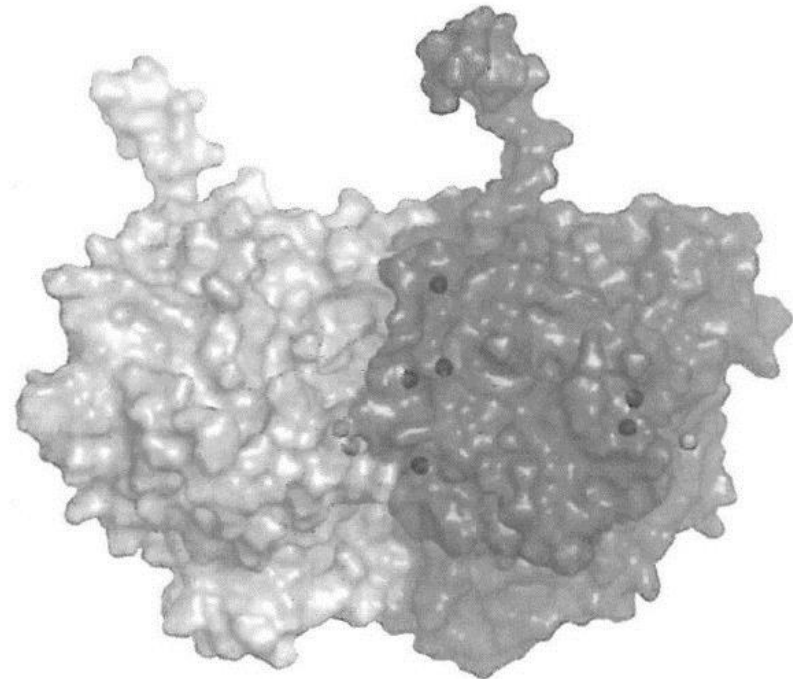
A**B**

Figure 3. Putative volatile anesthetic binding sites on the tubulin body. (A) 47 total sites (red spheres) with persistence ranging from 0.80% to 100%. (B) 9 most persistent, and probable, sites (orange spheres), with persistence of 70% or greater.
doi:10.1371/journal.pone.0037251.g003

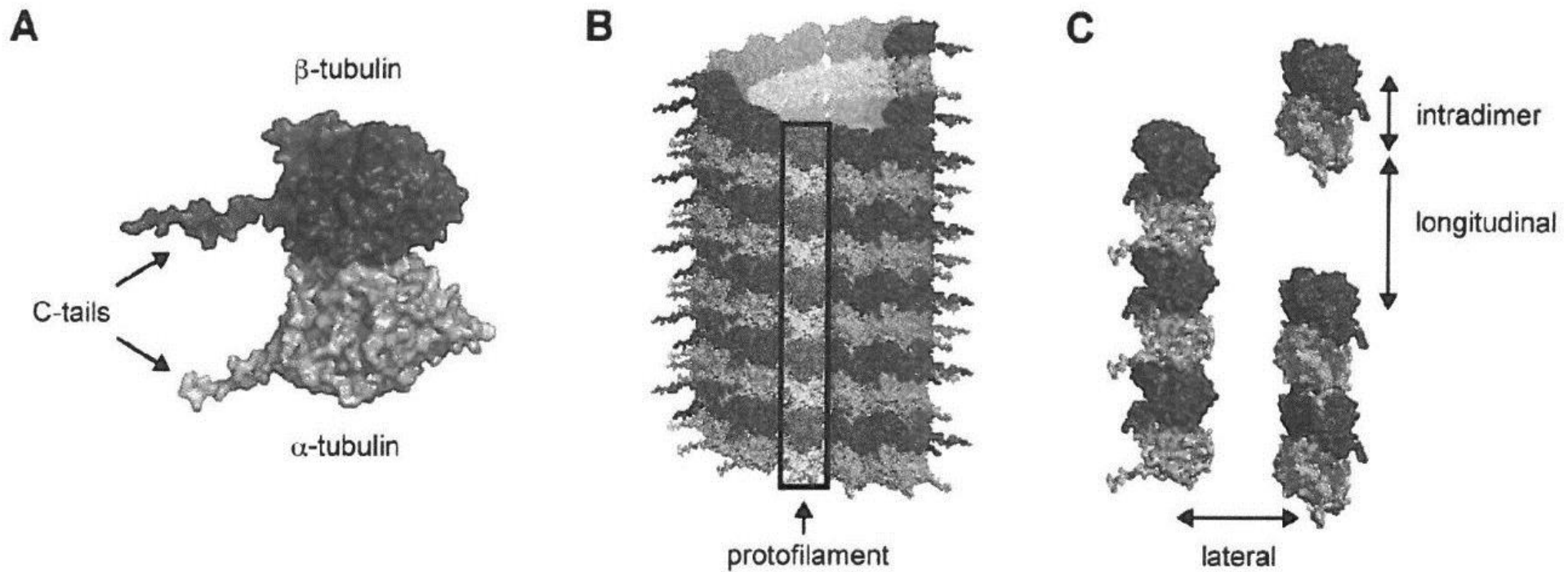
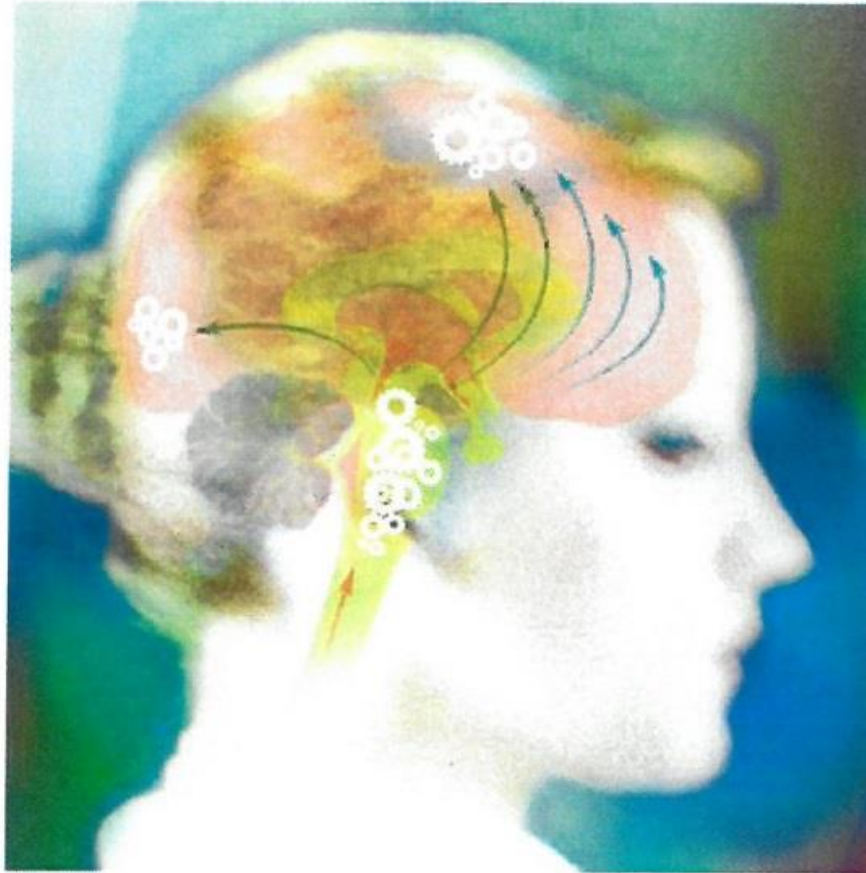


Figure 1. Tubulin in MT formation. (A) Tubulin dimer. Light grey – α -tubulin, Dark Grey – β -tubulin. C-terminal tails extend from the main tubulin body. (B) B-lattice MT with protofilament highlighted. (C) Tubulin interactions in MT formation. Intradimer – between α - and β -tubulins, Longitudinal – between dimers in a protofilament, Lateral – between protofilaments.

doi:10.1371/journal.pone.0037251.g001



“In which proteins do anesthetics act to erase consciousness?”